REMARKS

The application has been amended to indicate the proper claim to priority. The claim to priority of the parent application U.S. Application No. 09/161,122 has been amended in the Amendment filed September 5, 2002 in U.S. Application No. 09/161,122; a copy of the Amendment of September 5, 2002 is submitted herewith. Upon entry of the present amendment, the earliest date of priority is September 30, 1994.

Claims 1-40 were pending in this application. Claims 1-16, 19-21, 33 and 34 are withdrawn from consideration. Claims 41-48 have been added to more particularly point out what Applicants consider as the invention. Support for the new claims 41-48 can be found in the specification as set forth in the chart below. Support for the new claims can also be found in the earliest application to which the instant application claims priority see, for example, Example 9 of Serial No. 08/316,439. Thus, the new claims do not introduce new matter. Claims 1-48 will be pending upon entry of the present amendment.

Claim	Specification
41-43	page 20, lines 13-16
44	page 20, lines 8-12
45-47	page 20, line 20 to page 21, line 2
48	page 23, line 10 to page 26, line 25

THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, SHOULD BE WITH DRAWN

Claims 17-18, 22-32, and 35-40 are rejected under 35 U.S.C. § 112, first paragraph, because the specification allegedly fails to provide enablement for vaccine compositions that induce protective immunity in humans. The gravamen of the rejection is that the protective immunity in rodents and African green monkeys described in the present application is allegedly not predictive of RSV vaccine efficacy in humans. Applicants respectfully disagree. In response, Applicants assert that positive data obtained in accepted animal model systems *are* predictive of efficacy in humans.

Applicants submit that the description found in the specification as filed is adequate since the specification is enabled for vaccine compositions for inducing protective immunity in mammals other than humans. Under Section 112, it is not fatal that a certain

amount of experimentation may be required to adapt the invention to a specific purpose, provided the experimentation is routine. In re Wands, 858 F.2d 731, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988). Moreover, considerable amount of experimentation is permitted if it is merely routine or the specification provides a reasonable amount of guidance and direction to perform such experimentation. In re Jackson, 217 U.S.P.Q. 804, 807 (PTO Bd. Pt. App. Int. 1982).

Applicants submit that the specification contains an adequate description of the invention to enable the claims as currently pending. The provisions of Section 112, first paragraph, require that the description "enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same . . . (emphasis added). Applicants submit that any person skilled in the art of molecular biology can readily construct the chimeric viruses for use in vaccines as claimed by use of knowledge common in the art and in view of the teaching of the present specification. The specification also provides ample disclosure to allow one of skill in the art to assay the claimed vaccines to ensure that they are producing a protective immune response. See for example the specification of the instant application at page 108, line 25 to page 110, line2.

With regard to the Examiner's statement that the specification does not disclose detailed teachings for use of the vaccines of the invention in humans, Applicants point out that determining appropriate dosages and routes of administration is a matter of routine optimization that can be carried out using standard assays in the art. Moreover, the Examiner is respectfully reminded that the Court of Appeals for the Federal Circuit has held that testing for the full safety and effectiveness of a product is more properly left to the Food and Drug Administration and the requirements under the law for obtaining a patent should not be confused with the requirements for obtaining government approval to market a particular drug for consumption. *In re Brana*, 34 U.S.P.Q.2d 1437, 1442 (Fed. Cir. 1995); *see also Scott v. Finney*, 34 F.3d 1058, 1063 (Fed. Cir. 1994).

The Examiner alleges that eliciting antibody production in a mammalian host, other than a human, is not predictive for a protective immune response in humans. In response, the Applicants respectfully point out that the specification as originally filed discloses data demonstrating the protective capabilities of the present vaccines. Applicants respectfully invite the Examiner's attention to the instant specification at Example 13, page 105 to page 121. Example 13 demonstrates that the vaccines of the invention are effective in

of cotton rats (Table 21, page 118) and African Green monkeys (Table 22, page 119). The data presented in Table 21 also clearly correlate an increased neutralizing antibody titer with protective efficacy. Further, Applicants respectfully point out that the production of antibodies is a major part of the antigen-specific immune-response. The antibodies confer protection against infection. Once an organism has been exposed to an antigen and antibodies are made by B-cells, those B-cells are being kept in the organism as memory B-cells. So even if after the contact with the antigen, the antibody titer will decrease, the existence of memory B-cells will facilitate the response to a new infection. See for example Immunology and Inflammation, edited by Sigal and Ron, McGraw-Hill, Inc., 1994. Thus, as demonstrated by the successful application of the claimed vaccines to generate a protective immune response in two mammalian models, cotton rats and African green monkeys, the skilled artisan would also know how to use the vaccines of the present invention to achieve immunity.

An invention meets the standard for successful practice set by Section 112 unless the invention is "totally incapable of achieving a useful result." *Brooktree v. Advances Micro Devices*, 24 U.S.P.Q.2D 1401, 1412 (Fed. Cir. 1992). The Examiner's attention is directed to the opinion of the Court of Appeals for the Federal Circuit (Federal Circuit) in *In re Brana*, 34 U.S.P.Q.2d 1437 (Fed. Cir. 1995). In *Brana*, the Board had affirmed a final rejection under Section 112, 1st paragraph, of claims covering certain compounds asserted to be useful as anti-tumor substances because it was alleged that the specification was non-enabling since it did not sufficiently establish that the claimed compounds had a practical utility, *i.e.*, as anti-tumor agents. 34 U.S.P.Q.2d at 1439.

The Federal Circuit emphatically reversed the Board's decision. First, it explained the legal standard for compliance with the relevant Section 112 requirement, explaining that "unless there is reason to doubt the objective truth of the statements contained [in the specification] which must be relied on for enabling support", a specification's disclosure "must be taken as in compliance with the enabling requirement." *Id.* at 1441 (emphasis in the original). Further, the *Brana* Court made clear that the Patent and Trademark Office has the initial burden of challenging a presumptively correct assertion of utility; evidence must be presented that those of skill in the art would doubt the disclosure. Only then must the applicant provide rebuttal evidence.

Second, the Federal Circuit explained that even if one of skill in the art would have questioned the asserted utility, all applicants need do to overcome the rejection is to

proffer sufficient evidence to convince one skilled in the art of the asserted utility. *Id.* at 1441.

In the *Brana* situation, the Court found that the Patent and Trademark Office had not met its initial burden. Further, the Court held that even if the Patent and Trademark Office had met its burden, the evidence proffered was clearly sufficient to meet the statutory requirement. As explained by the Court:

> We hold as we do because it is our firm conviction that one who has taught the public that a compound exhibits some desirable pharmaceutical property in a standard experimental animal has made a significant and useful contribution to the art, even though it may eventually appear that the compound is without value in the treatment of humans.*Id.* at 1442 [quoting *In re Krimmel*, 292 F.2d 948, 953 (CCPA 1961)].

The Federal Circuit further reminded the Commissioner that testing for the full safety and effectiveness of a product is more properly left to the Food and Drug Administration and the requirements under the law for obtaining a patent should not be confused with the requirements for obtaining government approval to market a particular drug for consumption. 34 U.S.P.Q.2d at 1442; *see also Scott v. Finney*, 34 F.3d 1058, 1063 (Fed. Cir. 1994). In light of the *in vivo* rodent and primate protection data in the specification, the Examiner is clearly requiring human clinical testing in order to fulfill the enablement requirement. This standard is inappropriate under the law. *Brana, supra; Scott v. Finney, supra*. Moreover, it is unwarranted by the references cited by the Examiner, in contrast to the assertions in the Office Action.

The Examiner has relied on two references to support the allegation that eliciting antibody production in a mammalian host, other than a human, is not predictive of a protective immune response in humans: Bukreyer, 1997, *J. of Virol.* 71/12: 8973-8982 ("Bukreyer") and Murphy, 1994, *Virus Research* 32: 13-36 ("Murphy"). Bukreyer is cited for the proposition that the art *teaches* that an RSV vaccine may replicate *in vivo* and elicit protection from RSV challenge. Murphy is cited for the proposition that it is more difficult to protect a fully permissive host than it is to protect a semi-permissive host from RSV infection. The proffered evidence is *not* sufficient to meet the standard in Brana. Bukreyer merely describes the attenuated phenotype of an RSV mutant in mice and its ability to elicit a protective response. Murphy is merely reporting the differences in animal models for testing various subunit RSV vaccines. In fact, Murphy demonstrates that as of 1994, it was known

that while a vaccine may prove to elicit a protective effect in some animal models, repeated immunizations may be required to elicit an immune response in humans. In the instant case, the Applicant has demonstrated that the claimed vaccines will elicit a protective immune response in two mammalian models that are both art accepted models for demonstrating vaccine efficacy. There has been no evidence proffered to challenge the correct assertion of utility of the claimed vaccines to elicit an immune response. Thus, the rejection of the claims under 35 U.S.C. § 112, first paragraph, should be withdrawn.

The Examiner has further rejected the claims due to the alleged unpredictability and the quantity of experimentation required to practice the claimed invention. In response, the Applicants respectfully invite the Examiner's attention to section 2164.02 of the MPEP:

> "[...] if the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the examiner has evidence that the model does not correlate."

A vaccine gives rise to immunity to a particular pathogen in a subject. The generation of specific antibodies by the subject in response to administering the vaccine is one essential aspect of the immunity against the pathogen. Thus, it is an accepted view in the art that the generation of specific antibodies in response to administering a vaccine correlates with the generation of immunity against the pathogen.

Further, Applicants respectfully point out that procedures for testing a vaccine are routine in the art, and that the skilled artisan would be able to determine without undue experimentation which of the vaccines covered by the pending claims confer immunity to a subject when administered as a vaccine. In the context of this argument, the Applicants would like to direct the Examiner's attention to *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (citing *In re Angstadt*, 537 F.2d 489, 502-04, 190 USPQ 214, 217-19 (CCPA 1976)):

> " 'The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.' "

Thus screening procedures to test the vaccines of the invention for their potential to protect

not be considered undue experimentation since such procedures are well-known to the skilled artisan.

Applicants respectfully request that the rejections under 35 U.S.C. § 112, first paragraph, of claims 17-18, 22-32, and 35-40 should be withdrawn.

THE REJECTIONS UNDER 35 U.S.C. § 102 ARE OBVIATED BY THE AMENDMENT MADE HEREIN AND SHOULD THEREFORE BE WITHDRAWN

Claims 17-18, 22-32, and 35-40 were rejected under 35 U.S.C. 102(b) allegedly as being anticipated by Collins *et al.* (WO 97/12032; "Collins"). This rejection is in error and should be withdrawn.

Collins became available as prior art under 35 U.S.C. 102(b) on April 3, 1997. The priority date of the instant application, as amended herein, is September 30, 1994 and predates Collins. Thus, Collins is not available as art to the instant application and the applicants respectfully submit that the rejection under 35 U.S.C. § 102(b) should be withdrawn.

Further, claims 17-18, 22-32, and 35-40 were rejected under 35 U.S.C. 102(e) allegedly as being anticipated by Murphy *et al.* (U.S. Patent 5,993,824; "Murphy"). This rejection is in error and should be withdrawn.

Murphy was filed on July 15, 1997 and appears to claim the benefit of priority of three provisional applications, the earliest of which was filed on July 15, 1996. The earliest possible 102(e) date of Murphy is therefore July 15, 1996. The priority date of the instant application, however, is September 30, 1994 and predates Murphy. Thus, Murphy is not available as art to the instant application and the applicants respectfully submit that the rejection under 35 U.S.C. § 102(e) should be withdrawn.

THE REJECTION UNDER 35 U.S.C. § 103(a) IS OBVIATED BY THE AMENDMENT MADE HEREIN AND SHOULD THEREFORE BE WITHDRAWN

Claims 17-18, 22-32, and 35-40 are rejected under 35 U.S.C. § 103(a) allegedly as being obvious over Collins *et al.*, 1995 (Proc. Natl. Acad. Sci. 92:11563-11567; "Collins, 1995") in view of Olmsted *et al.* (Proc. Natl. Acad. Sci. 83:7462-7466, 1986; "Olmsted"). This rejection is in error and should be withdrawn.

Collins, 1995 became available as prior art for 35 U.S.C. 103(a) in December 1995. The priority date of the instant application, as amended herein, is September 30, 1994 and predates Collins, 1995. The rejection of claims 17-18, 22-32, and 35-40 under 35 U.S.C. § 103(a) depends on the combination of Collins, 1995 with Olmsted. As Collins, 1995 is not available as art to the instant application, applicants respectfully submit that the rejection under 35 U.S.C. § 103(a) should be withdrawn.

Conclusion

Applicants respectfully request entry and consideration of the foregoing amendments and remarks. No new matter has been introduced. The claims are believed to be free of the art and patentable. Withdrawal of all the rejections and an allowance are earnestly sought.

Respectfully submitted,

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Enclosures